

## Changes of progesterone concentrations in blood plasma of sows during periparturient period

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### ABSTRACT

Changes of progesterone level in a total of 40 parturient sows were investigated from the fourth to the second day prior to parturition (phase A), at parturition (phase B) and on the second day post-parturition (phase C). Venepuncture was performed on the vena cava cranialis by means of a needle and a syringe. Blood samples were collected in test tubes containing heparin. The radioimmunoassay method of direct quantitative measurement of the progesterone level in plasma was applied. Concentrations of progesterone in phase A ranged between 0.2 and 50.1 nmol/l, with a mean value of 18.14 nmol/l. At parturition (phase B) the level of progesterone ranged between 1.1 and 27.4 nmol/l (6.09 nmol/l), and in phase C the mean level of progesterone was 2.68 nmol/l (0.6-8.1 nmol/l). Results of measurements showed a drop in blood plasma concentrations. Lowest values were recorded on the second day post-parturition, which led to the conclusion that progesterone levels display a constant downward trend from the fourth day prior to parturition until the second day post-parturition. The greatest differences were observed during the pre-parturition period, whereas only two days into parturition they were statistically negligible (standard deviation 1.61).

**Key words:** progesterone, gilt, sow, periparturient, parturition, parturient

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## Introduction

Although basically under the control of LH (JAINUDEN and HAFEZ, 1987; CAROLA et al., 1990), the regulation of progesterone secretion has not yet been completely established. The highest level of progesterone in blood is in the pregnancy stage, since placenta – being a new organ – secretes amounts several times greater (MEYER, 1994). The neurohormonal stimulation initiated by a pregnant uterus brings about continuous LH secretion, maintained by corpus luteum (ROBERTS, 1971). Moreover, BARNES et al. (1974) reported that it is the corpus luteum that is crucial for maintenance of pregnancy in sows and that extraovarial progesterone alone is not enough. This was proved by experiments in which ovariectomy was performed on pregnant sows (PARVIZI et al., 1976), the gestation of which could not be maintained.

As indicated by CSAPO (1956) and ARTHUR et al. (1992), the domination of progesterone (progesterone “block”) continues until oxytocin starts secreting, since progesterone itself has no effect on oxytocin receptors (“see-saw” theory, CSAPO, 1977). THORBURN (1979) calls it miometrial blockator. That is to say, unlike oestrogen, progesterone obstructs the synthesis of oxytocin receptors (FLINT and SHELDRIK, 1982), which means that the pre-parturition drop in progesterone can eventually result in an increase in oestrogen receptors (GIBB and RANDALL, 1992).

After having accidentally administered prostaglandin (altrenogest) instead of *E. coli* vaccine to 11 sows 3-6 weeks prior to anticipated parturition, DESBORDES et al. (1991) confirmed that progesterone is a gestational hormone. Pregnancy was maintained to end of term in 81% of sows.

WHITELY et al. (1990) managed to postpone parturition by administering medroxyprogesterone acetate (MPA) to all sows except those in the control group. The pregnancy of treated sows lasted significantly longer (two days).

DZIUK (1979) and GEREŠ (1997) reported that the level of progesterone in maternal plasma gradually decreased prior to parturition, thus allowing a higher concentration of other hormones (oestrogens, cortisol, relaxin). This occurred 24-30 hours subsequent to the administration of PGF<sub>2</sub> (SILVER, 1992), which means that after the 111<sup>th</sup> day of pregnancy, prostaglandin is capable of inducing parturition. DIEHL and NEWBY (1988) also treated pregnant sows with analogues of PGF<sub>2</sub>. The interval preceding whelping was shortened and the level of progesterone dropped from 0.036 nmol/l to 0.02 nmol/l. ANDERSON

(1987) reported that the mean value of progesterone in sows immediately prior to parturition was 0.002 nmol/l.

HOFIG et al. (1988) induced whelping by means of antigestagen ZK 112.993, which they administered just prior to parturition. This procedure was soon followed by a normal parturition, due to the sudden drop in the progesterone level.

WILSON et al. (1989) studied the effects of progesterone in 21 heavily gravid gilts. They were all exogenously administered progesterone between the 108<sup>th</sup> and 113<sup>th</sup> day of pregnancy. Unlike those in the control group, no decrease in concentration was observed in experimental sows, although on the 114<sup>th</sup> day it increased. Parturition occurred on the 115<sup>th</sup> ±0.3 days and the percentage of live births was low. The concentration of progesterone decreased in the gilts treated with prostaglandin F<sub>2</sub> on the 114<sup>th</sup> day of pregnancy, although pregnancy duration was about the same but with a lower percentage of live births. The authors assumed that exogenous administration of progesterone to sows during the periparturient period might stimulate continuous endogenous secretion. This experiment did not include measurement of the level of progesterone at parturition.

The level of progesterone in the non-placental regions in sows increased in the early stage and decreased both in the late stage of pregnancy and at parturition (THILANDER et al., 1990; GEREŠ, 1997).

BALDWIN and STABENFELDT (1975) and ELLENDORFF et al. (1979) found that the level of corticosteroids in sows increased rapidly 24 hours prior to parturition and then decreased during the early stage of lactation, which was accompanied by a simultaneous drop in the progesterone level just prior to parturition. Regardless of the level to which an increase in cortisol can be stimulated by application of dexamethasone, this did not help inducing the parturition in those cases in which the level of progesterone was preserved (COGGINS et al., 1977; SILVER, 1992).

The aim of this work was to investigate changes in the progesterone level in blood plasma in a total of 40 periparturient sows in period from the fourth to the second day prior to parturition, at parturition and on the second day following parturition, and proved existing evidence that levels of progesterone have a downward trend, particularly following parturition.

## **Materials and methods**

The investigation was initiated at the farrowing department of the "Sljeme" pig farm in Sesvete, Croatia. Having taken the average duration

of pregnancy ( $114 \pm 1$  day) as the key criterion, venepuncture was performed on 76 parturient sows 4-2 days prior to anticipated parturition. Further treatment included taking of blood samples from 40 parturient sows, of which 7 were gilts. They actually farrowed 4-2 days after the first venepuncture (phase A). The second venepuncture, which we designated as phase B, was performed on the day of parturition (at its initial stage) and the third took place two days post-parturition (phase C), exactly 48 hours later.

Venepuncture was performed on the vena cava cranialis by means of a needle and a syringe. Blood samples (3 ml) were collected in test tubes containing heparin. The test tubes were immediately centrifuged for ten minutes at 3000 rpm. The plasma was then isolated in polystyrene tubes and stored at  $-20$  °C.

The radioimmunoassay (RIA) method of direct quantitative measurement of the progesterone level in plasma was applied *in vitro*, without extraction procedure, by means of PROG-CTK-3 (manufactured by Sorin-Biomedica, Milan, Italy). All tests were performed in duplicate ( $120 \times 2$ ) to ensure high reliability and good control of results. Concentrations are given in nmol/l.

Table 1. Changes in progesterone concentrations (nmol/l)  
in blood plasma in sows in phases A, B, C

| Progesterone | Samples | Mean value | Min. value | Max. value | SD    |
|--------------|---------|------------|------------|------------|-------|
| Phase A*     | 40      | 18.15      | 0.2        | 50.1       | 10.58 |
| Phase B**    | 40      | 6.09       | 1.1        | 27.4       | 5.93  |
| Phase C***   | 40      | 2.68       | 0.6        | 8.1        | 1.61  |

\* 4-2 days prior to parturition; \*\* on the day of parturition; \*\*\* 2 days after parturition

Concentrations of progesterone in all three phases are shown in Tables 1, 2, 3 and in figures 1 and 2. All values of progesterone were ranged from the lowest to the highest, with mean values and standard deviation in all phases being analysed by Student's t-test for small dependent samples and Wilcoxon s test doubles of variables.

## Results

Values of progesterone in phase A ranged from the lowest of (sow No. 17) 0.20 nmol/l to the highest (No. 4) of 50.1 nmol/l, with a mean value of 18.15 nmol/l and standard deviation of 10.58. The lowest concentration of progesterone in phase B was found in parturient sow No.

29 (1.10 nmol/l) and the highest in No. 24 (27.40 nmol/l). Mean value was 6.09 nmol/l, while standard deviation was 5.93 (Fig. 1.).

Table 2. T-test for small dependent samples for progesterone concentrations (nmol/l) in blood plasma in sows in phases A, B, C

|            | nmol/l | SD    | N  | Difference | SD difference | t    | P       |
|------------|--------|-------|----|------------|---------------|------|---------|
| Phase A*   | 18.15  | 10.58 | 40 | 12.06      | 11.04         | 6.91 | 0.00001 |
| Phase B**  | 6.09   | 5.93  |    |            |               |      |         |
| Phase A*   | 18.15  | 10.58 | 40 | 15.47      | 10.49         | 9.33 | 0.00001 |
| Phase C*** | 2.67   | 1.61  |    |            |               |      |         |
| Phase B**  | 6.09   | 5.93  | 40 | 3.42       | 4.82          | 4.48 | 0.00006 |
| Phase C*** | 2.67   | 1.61  |    |            |               |      |         |

\* 4-2 days prior to parturition; \*\* on the day of parturition; \*\*\* 2 days after parturition

The highest level of progesterone in phase C was found in parturient sow No. 26 (8.1 nmol/l) and the lowest in No. 20 (0.6 nmol /l).

Table 3. Wilcoxon's test doubles of variables of progesterone concentrations (nmol/l) in blood plasma in sows in phases A, B, C

| Doubles of variables progesterone | N  | T  | Z    | P        |
|-----------------------------------|----|----|------|----------|
| Phases A* and B**                 | 40 | 43 | 4.93 | 0.000001 |
| Phases A* and C***                | 40 | 6  | 5.43 | 0.000001 |

\* 4-2 days prior to parturition; \*\* on the day of parturition; \*\*\* 2 days after parturition

The mean value of progesterone in gilt No. 10 was lower in phase A than in phase B (13.80 nmol/l: 16.20 nmol/l), whereas in sows No. 17 and 25 it was somewhat higher in phase C than in phase A.

All other pigs possessed peak values in phase A, showing a constant tendency to decrease towards phase C.

Standard deviations (SD) showed great dispersal of data in all three phases since their range was wider than +3SD, although Lilliefors distribution test showed patterned distribution. Student's t-test for small, dependent samples showed a statistically significant difference between measurements, as shown in Table 2. The t-test value in phase A, compared to phase B, was  $t=6.91$  ( $P<0.001$ ), for phases A and C it was

$t=9.33$  ( $P>0.001$ ) and for phases B and C  $t=4.448$  ( $P>0.001$ ). (Table 3., Fig. 2.).

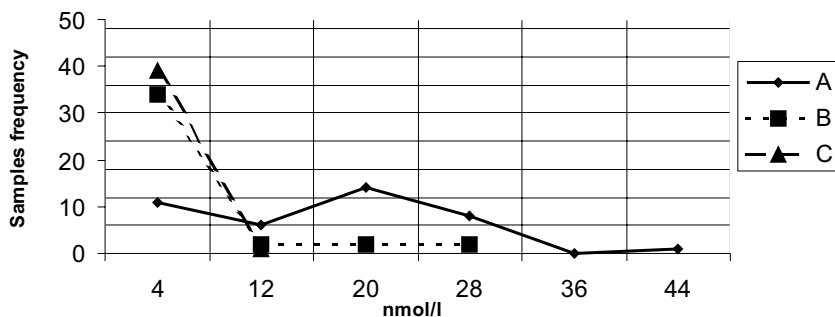


Fig. 1. Changes in progesterone concentrations in blood plasma in sows in phases A (4-2 days prior to parturition), B (on the day of parturition), C (2 days after parturition)

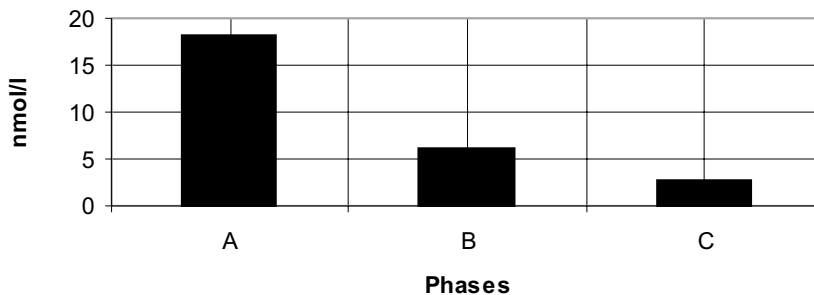


Fig. 2. Mean values of samples of progesterone concentrations (nmol/l) in blood plasma in sows in phases A (4-2 days prior to parturition), B (on the day of parturition), C (2 days after parturition)

## Discussion

Concentrations of progesterone in phase A, i.e. 4-2 days prior to parturition, varied from the lowest of 0.2 nmol/l (No. 17) to the highest of 50.1 nmol/l (No. 4). Such a high concentration in sow No. 4 can be explained by the fact that venepuncture was performed four days prior to parturition when the level of progesterone had not then taken a downward trend. ROBERTSON and KING (1974) found that the mean level of progesterone in sows was 47.17 nmol/l four days prior to parturition.

ANDERSON (1987) measured the level of progesterone on the 104<sup>th</sup> day of pregnancy, which ranged between 63.6 and 79.5 nmol/l. ADAIR et al. (1989) found that the mean level of progesterone in the periparturient period drops to half its value (52.47 nmol/l). BASSET et al. (1969), BEDFORD et al. (1972) and STABENFELDT (1972) reported that a considerable decrease occurs at 5-15 days, being followed by a definite decrease at parturition. The highest level was recorded by WILSON et al. (1989) on the 114<sup>th</sup> day of pregnancy amounting to  $92.86 \pm 36.25$  nmol/l. According to ARTHUR et al. (1992) these levels were somewhat lower six days prior to parturition (28.62 nmol/l), whereas SZAFRANSKI and TILTON (1993) found that concentrations of progesterone preceding the periparturient decrease ranged between 40.06 and 66.14 nmol/l.

The level of progesterone in sow No. 32 also departed significantly from mean values (41.10 nmol/l); venepuncture had been performed two days prior to parturition, as with sows No. 24 (31.40 nmol/l) and No. 39 (30.60 nmol/l), blood samples from which had been taken three days earlier. Progesterone levels were higher in these three parturient sows than in the majority of others, thus indicating that a periparturient decrease in progesterone level did not occur. TAVERNE et al. (1978/79) obtained a mean value of 45.70 nmol/l three days prior to parturition, and DIEHL and NEWBY (1988) reported 31.48 nmol/l two days prior to parturition.

According to PLONAIT and BICKHARDT (1988), imminent parturition is indicated by occurrence of corticosteroids that are stimulated by an unidentified pituitary factor on the part of the foetus. This causes the production of prostaglandin F<sub>2</sub>, consequential luteolysis and drop in progesterone concentration. GIBB and RANDALL (1992) believe that cortisol could be one of the factors responsible for the weakened production of progesterone from allantochorion before sows go into labour.

It is not yet completely clear how progesterone converts into oestrogen in sows (we know how this mechanism works only with sheep) before they go into labour, despite the fact that 3 $\beta$ -hydroxysteroid dehydrogenase and aromatase cause the withdrawal in progesterone level in the maternal plasma, thus giving way to an increase in levels of other hormones (FLINT et al., 1979).

The levels of progesterone in sows Nos. 9, 10, 24, 25, 26 and 32 were above 10 nmol/l on the day of parturition. This agrees with results obtained by TAVERNE et al. (1978/79), their mean concentration being 11.93 nmol/l. In other experimental sows the level of progesterone measured on the day of parturition ranged between 1.10 to 7.70 nmol/l,

which is in agreement with the data obtained by ELLENDORF et al. (1979), who claimed that the concentration fell below 10 nmol/l. ANDERSON (1987) recorded 1.59 nmol/l and ARTHUR et al. (1992) 4.77 nmol/l. TSUMA et al. (1995) measured the level of progesterone in 9 pigs in the period between three days prior to parturition to three days post-parturition, where it ranged between 0.4–1.4 nmol/l.

Our results proved that the progesterone level decreases rapidly just prior to parturition. DZIUK (1979) found that this decrease is due to the effects of PGF<sub>2</sub> and that it occurs 29 hours prior to parturition. Normal subsequent parturition is due to an absence of progesterone (HOFIG et al., 1988). SILVER et al. (1979) stated that the rapid decrease in progesterone occurs 24 hours prior to parturition, whereas MEUNIER-SALAUN et al. (1991) found that this decrease occurs 48 hours prior to parturition as a result of the previous increase in the cortisol level.

The levels of progesterone in phase C prove a definitive decrease in progesterone after parturition. The mean concentration value in phase C of our experiment amounted to 2.68 nmol/l, which is significantly lower than that recorded in phase B (6.09 nmol/l).

The results correspond to those obtained by ROBERTSON and KING (1974), ASH and HEAP (1975) and TAVERNE et al. (1978/79), who measured levels of progesterone two days into parturition to the amount of 2.39 nmol/l and ANDERSON (1987) who recorded 1.59 nmol/l. SMITH et al. (1992) measured the level of progesterone in the period from 2 days prior to parturition until 7 days post-parturition, their mean concentrations ranging between 0.95 and 1.27 nmol/l. The results correspond with the final luteolysis stage.

We can also explain the deviations in results obtained by measurement of progesterone levels in parturient pigs in phase B by the fact that venepunctures were performed on the day of parturition, but not in equal intervals, as was the case at the beginning of parturition. The rate of progesterone level decrease is not always constant, due to regression of corpus luteum (CAMPBELL et al., 1994).

In conclusion, the levels of progesterone, starting with the fourth day prior to parturition, show a downward trend. The greatest differences occurred in phase A, whereas in phase C their significance was negligible (SD 1.61).

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**GEREŠ, D., D. ŽUBČIĆ, D. SABO, A. PLELI, P. DŽAJA, D. MIHELIĆ, G. MÜLLER:**  
**Promjene razina progesterona u krvnoj plazmi krmača u peripartalnom**  
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**SAŽETAK**

Istraživane su promjene razina progesterona u 40 krmača porodilja u peripartalnom razdoblju, od 4 do 2 dana prije porođaja (faza A), u vrijeme porođaja (faza B) i dva dana poslije porođaja (faza C). Krv za analizu uzeta je venepunkcijom iglom iz kranijalne šuplje vene uz uporabu heparina kao antikoagulansa. Korištena je radioimunološka metoda direktnog kvantitativnog mjerenja razine progesterona u plazmi. Koncentracije progesterona u fazi A kretale su se u rasponu od 0,2 do 50,1 nmol/l, uz srednju vrijednost 18,15 nmol/l. U vrijeme porođaja (faza B) razine progesterona bile su od 1,1 nmol/l do 27,4 nmol/l (6,09 nmol/l). U fazi C srednja je razina progesterona bila 2,68 nmol/l (0,6-8,1 nmol/l). Rezultati mjerenja ukazali su na pad razine progesterona s najnižim vrijednostima dva dana poslije porođaja. Autori su zaključili da su razine progesterona od četvrtog dana prije porođaja do drugog dana poslije porođaja imale kontinuirani pad. Najveće razlike bile su u razdoblju prije porođaja da bi već dva dana poslije bile bez signifikantnosti (SD 1,61).

**Ključne riječi:** progesteron, nazimica, krmača, peripartalno razdoblje, porođaj

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